

Claims

1. A method to deliver a desired agent selectively to a target site in a subject, which method comprises administering, substantially simultaneously, to said subject:

(1) an active composition of targeted particulate vehicles wherein said vehicles are coupled to a ligand that binds specifically to its cognate at the target site and wherein said vehicles comprise, or are themselves, the agent to be delivered; and

(2) an inactive carrier which comprises particulate vehicles which lack said binding ligand and which optionally lack said agent;

wherein the ratio of vehicles in the carrier of (2) to vehicles in the composition of (1) is sufficient to enhance the association of the active composition with target site, and/or to lower the required dosage of targeted vehicles.

2. The method of claim 1 wherein the ratio of vehicles in the carrier (2) to vehicles in the composition of (1) is at least 1:1.

3. The method of claim 1 wherein the ratio of vehicles in the carrier (2) to vehicles in the composition of (1) is at least 100:1.

4. The method of claim 1 wherein the vehicles comprise liposomes, micelles, bubbles containing gas and/or gas precursors, lipoproteins, halocarbon and/or hydrocarbon nanoparticles, halocarbon and/or hydrocarbon emulsion droplets, hollow and/or porous particles and/or solid nanoparticles.

5. The method of claim 1 wherein the vehicles in the carrier of (2) and the vehicles in the composition of (1) are of the same composition.

6. The method of claim 1 wherein the vehicles in the carrier of (2) and the vehicles in the composition of (1) are not of the same composition.

7. The method of claim 1 wherein either the carrier of (2) or the composition of (1) or both is comprised of vehicles that are not of the same composition.

8. The method of claim 1 wherein at least one said agent is selected from the group consisting of a contrast agent for ultrasound; a magnetic resonance imaging (MRI) agent; a radionuclide; a therapeutic agent; and a fluorophore.

9. The method of claim 1 wherein the ligand that binds to cognate is an antibody or fragment thereof or is a peptidomimetic.

10. The method of claim 9 wherein said moiety targets $\alpha_v\beta_3$.

11. A formulation which comprises

(1) an active composition of particulate targeted vehicles wherein said vehicles are coupled to a ligand that binds specifically to a cognate at a target site and wherein said vehicles comprise, or are themselves, an agent to be delivered to said target site; and

(2) an inactive carrier which comprises particulate vehicles which lack said binding ligand and which optionally lack said agent.

12. The formulation of claim 11 wherein the ratio of vehicles in the carrier of (2) to vehicles in the composition of (1) is sufficient to enhance the association of the active composition with the target site and/or to lower the required dosage of targeted vehicles.

13. The formulation of claim 11 wherein the ratio of vehicles in the carrier of (2) to vehicles in the composition of (1) is at least 1:1.

14. The formulation of claim 11 wherein the ratio of vehicles in the carrier of (2) to vehicles in the composition of (1) is at least 100:1.

15. The formulation of claim 11 wherein the vehicles comprise liposomes, micelles, bubbles containing gas and/or gas precursors, lipoproteins, halocarbon and/or hydrocarbon nanoparticles, halocarbon and/or hydrocarbon emulsion droplets, hollow and/or porous particles and/or solid nanoparticles.

16. The formulation of claim 11 wherein the vehicles in the carrier of (2) and the vehicles in the composition of (1) are of the same composition.

17. The formulation of claim 11 wherein the vehicles in the carrier of (2) and the vehicles in the composition of (1) are not of the same composition.

18. The formulation of claim 11 wherein either the carrier of (2) or the composition of (1) or both is comprised of vehicles that are not of the same composition.

19. The formulation of claim 11 wherein at least one said agent is selected from the group consisting of a contrast agent for ultrasound; a magnetic resonance imaging (MRI) agent; a radionuclide; a therapeutic agent; and a fluorophore

20. The formulation of claim 11 wherein the moiety that binds to cognate is an antibody or fragment thereof or is a peptidomimetic.

21. The formulation of claim 20 wherein said moiety targets $\alpha_v\beta_3$.

22. A method to obtain an ultrasound image of a targetable site, which method comprises obtaining said image in a subject, wherein said subject has been administered, substantially simultaneously,

(1) an active composition of particulate targeted vehicles wherein the vehicles are coupled to a ligand that binds specifically to a cognate at the target site and comprise an ultrasound contrast agent, and

(2) an inactive carrier which comprises vehicles that lack said binding ligand, in a ratio of vehicles in the carrier of (2) to vehicles in the active composition of (1) which is sufficient to enhance the association of the active composition with the target site, and/or to lower the required dosage of targeted vehicles.

23. The method of claim 22 wherein the vehicles in the active composition are perfluorocarbon nanoparticles and the vehicles in the inert carrier are oil droplets.

24. A method to obtain a proton magnetic resonance image of a target site in a subject which method comprises obtaining said image from a target in a subject that has been administered, substantially simultaneously,

(1) an active composition of particulate targeted vehicles wherein said vehicles are coupled to a ligand that binds specifically to a cognate at the target site and comprise a chelating agent containing a heavy metal ion; and

(2) an inactive carrier which comprises vehicles which lack said binding ligand and optionally lack said heavy metal ion,

wherein the ratio of vehicles in the carrier of (2) to the vehicles in the active composition of (1) is sufficient to enhance the association of the active composition with the target site, and/or to lower the required dosage of targeted vehicles.

25. The method of claim 24 wherein the chelating agent comprises DOTA and the binding moiety binds to $\alpha_v\beta_3$.

26. A method to obtain an optical image of a target site, which method comprises obtaining said image in a subject, wherein said subject has been administered, substantially simultaneously,

(1) an active composition of particulate targeted vehicles wherein the vehicles are coupled to a ligand that binds specifically to a cognate at the target site and comprise a visible label, and

(2) an inactive carrier which comprises vehicles that lack said binding ligand, in a ratio of vehicles in the carrier of (2) to vehicles in the active composition of (1) sufficient to enhance the association of the active composition with the target site, and/or to lower the required dosage of targeted vehicles.

27. The method of claim 26 wherein the visible label is fluorescent and the inactive carrier lacks said label.

28. A method to obtain an X-ray image of a target, which method comprises obtaining said image in a subject, wherein said subject has been administered, substantially simultaneously,

(1) an active composition of particulate targeted vehicles wherein the vehicles are coupled to a ligand that binds specifically to a cognate at the target site and comprise at least one X-ray opaque ligand, and

(2) an inactive carrier which comprises vehicles that lack said binding ligand, in a ratio of vehicles in the carrier of (2) to vehicles in the active composition of (1) sufficient to enhance the association of the active composition with the target site, and/or to lower the required dosage of targeted vehicles.

29. The method of claim 28 wherein the vehicles in the inactive carrier lack said opaque moiety.

30. A method to obtain ^{19}F magnetic resonance image of a target, which method comprises obtaining said image in a subject, wherein said subject has been administered, substantially simultaneously,

(1) an active composition of particulate targeted vehicles wherein the vehicles are coupled to a ligand that binds specifically to a cognate at the target site and comprise ^{19}F , and

(2) an inactive carrier which comprises vehicles that lack said binding ligand, in a ratio of vehicles in the carrier of (2) to vehicles in the active composition of (1) sufficient to enhance the association of the active composition with the target site, and/or to lower the required dosage of targeted vehicles.

31. The method of claim 30 wherein the vehicles in the active composition are perfluorocarbon nanoparticles and the vehicles in the inactive carrier are oil droplets.